European Journal of Clinical Microbiology & Infectious Diseases (2024) 43:1383–1392
https://doi.org/10.1007/s10096-024-04835-6

RESEARCH

Epidemiology and antimicrobial resistance patterns of bacterial meningitis among hospitalized patients at a tertiary care hospital in Saudi Arabia: a six-year retrospective study

Abdulaziz H. Alhazmi[1] · Khalid M. Alameer[1] · Bandar M. Abuageelah[2] · Amal Yahya Gharawi[1] · Ehab Farouq Hakami[1] · Taif Ali Zogel[1] · Abdullah Jaber Almalki[1] · Ebhar Gubran Magrashi[1] · Wafa Ali Alharbi[1] · Ramis Mohammed Manni[1] · Atheer Ali Buayti[1] · Ahmad A. Alharbi[1] · Nabil S. Dhayhi[3] · Moayad Haddad[3]

Received: 7 March 2024 / Accepted: 22 April 2024 / Published online: 29 April 2024

Abstract

Introduction Bacterial meningitis poses significant medical challenges due to its acute inflammatory nature and potential for severe neurological complications, emphasizing the need for prompt diagnosis and treatment. Limited data exists on its epidemiology and antimicrobial resistance trends among hospitalized patients in Saudi Arabia. This study aimed to investigate these factors at a tertiary care hospital over six years.

Methods A retrospective analysis was conducted on cerebrospinal fluid samples results from 222 bacterial meningitis cases among hospitalized patients between 2018 and 2023. Demographic, clinical, microbiological data, and antibiotic susceptibility patterns were collected and analyzed.

Results Pseudomonas aeruginosa (43%) was the predominant pathogen isolated. Neonates (16%) and children (47%) were most affected population. Nosocomial meningitis accounted for 92% of cases, mainly in the intensive care settings (50.45%). Extended-spectrum beta-lactamase was the leading resistance pattern (12.2%). Seasonal variation was observed, with a peak incidence in October-November.

Conclusion The study highlights the substantial burden of bacterial meningitis among hospitalized patients, especially among high-risk groups. Emerging antimicrobial resistance emphasizes the need for optimized surveillance and stewardship. Future prospective research employing molecular techniques across multiple centers in the country is warranted to enhance understanding and guide public health strategies in Saudi Arabia.

Keywords Bacterial meningitis · Gram-negative · Antimicrobial resistance · Nosocomial infections · Saudi Arabia

Introduction

Bacterial meningitis, characterized by acute inflammation of the meninges, subarachnoid space, and brain vasculature due to infection, represents a critical medical condition necessitating urgent attention [1]. This illness is associated with severe neurological complications, requires early diagnosis and prompt treatment initiation, and often leads to hospitalization in intensive care units (ICUs) [2, 3]. The clinical presentation of meningitis commonly features a classic triad of symptoms, including fever, meningismus (headache, neck stiffness, and photophobia), and altered mental state. Additional potential manifestations among hospitalized individuals may encompass nausea, vomiting, malaise, and seizures. In neonates and young children, symptoms are frequently nonspecific or subtle, posing challenges in confirming a definitive diagnosis [4, 5]. In pediatric populations, the incidence of meningitis is most prevalent among children under the age of 1, while in adults, the median age of onset is around 43 years [6, 7]. Over the past two decades,

✉ Abdulaziz H. Alhazmi
abalhazmi@jazanu.edu.sa

[1] Faculty of Medicine, Jazan University, Jazan 45142, Saudi Arabia

[2] Department of Medicine and Surgery, Batterjee Medical College, Aseer 62451, Saudi Arabia

[3] King Fahad Central Hospital, Ministry of Health, Jazan 45142, Saudi Arabia

Western countries have witnessed a gradual decrease in the incidence of community-acquired bacterial meningitis, with rates declining by approximately 3–4% annually to reach 0.7–0.9 cases per 100,000 individuals yearly. In contrast, African nations continue to experience significantly higher incidence rates ranging from 10 to 40 cases per 100,000 persons annually [8]. The specific community incidence of bacterial meningitis in Saudi Arabia remains elucidated based a national registry, especially when it comes to hospital settings.

In developed nations, nosocomial meningitis makes up 40% of bacterial meningitis cases and is linked to high mortality and morbidity rates because of severe clinical outcomes [2, 9]. Invasive medical procedures such as craniotomy, external ventricular drains (EVD), external lumbar catheters, and lumbar punctures, in addition to moderate to severe head trauma, subarachnoid hemorrhage, and occasionally infections in patients with bacteremia, are contributing factors [10–14]. Individuals who are undergoing subarachnoid hemorrhage, tumor neurosurgery, or severe traumatic brain injury (TBI) are most susceptible to developing postoperative meningitis [9].

Multiple pathogens, including bacteria, viruses, fungi, and parasites, can give rise to central nervous system (CNS) infections, such as meningitis. As diagnostic tools for CNS infections evolve, the BioFire FilmArray Meningitis/Encephalitis Panel has emerged as a promising alternative to traditional CSF cultures, which have long been considered the "gold standard" in diagnosing CNS infections [15]. The culture of CSF is functional for bacterial meningitis. However, it has an extended processing time and may be affected by prior empiric antibiotic administration, timing of lumbar puncture (LP), and volume of CSF collected [16]. Viral cultures are considered the gold standard for detecting viable viruses. Viral isolates from clinical samples allow further virulence and antiviral drug resistance analysis. However, viral cultures have limitations, such as low yield for some viruses, suboptimal sensitivity, and the need for the technical expertise of well-trained technologists. Therefore, molecular tests have replaced viral cultures in most clinical virology labs [17, 18].

Given the significant burden of morbidity and mortality associated with bacterial meningitis globally, obtaining accurate data on the critical causative agents and high-risk populations is crucial for implementing effective public health measures and providing optimal treatment [19]. Continuous evaluation of bacterial meningitis worldwide is essential due to the variability of infectious agents over time, across different regions, and among various age groups [20]. Considering the limited research on the etiology and epidemiology of bacterial meningitis either as community or hospital acquired infections in Saudi Arabia, there is a need for comprehensive studies in this area. Therefore, our study was conducted to investigate the diverse epidemiological factors associated with bacterial meningitis among hospitalized patients over six years from 2018 to 2023 at a tertiary hospital in Saudi Arabia.

Materials and methods

Study design and settings

A retrospective analysis was carried out at, King Fahad Central Hospital (KFCH) a tertiary hospital in Jazan, Saudi Arabia, on all cerebrospinal fluid (CSF) samples from hospitalized and suspected cases of meningitis submitted to the microbiology laboratory between January 2018 and November 2023. The hospital functions as the designated referral center for the region, strategically situated amidst 13 adjacent regions. Boasting a bed capacity of 500, this hospital stands as the exclusive facility for neurosurgeries within the region, holding regional prominence for leadership in healthcare quality and patient safety.

Inclusion and exclusion criteria

Hospitalized patients of all ages, both male and female, who were diagnosed with bacterial meningitis between January 2018 and October 2023 at KFCH were included in the study. Patients diagnosed in 2023 who remained hospitalized at the time of data collection in November 2023 were included. However, their length of stay was incalculable due to ongoing admission. Thus, we classified their length of hospital stay as not determined (ND). Patients diagnosed with viral or aseptic meningitis and those with central nervous system tuberculosis (CNS TB) infections were excluded based on clinical findings and CSF test results. Additionally, patients with incomplete medical records regarding demographic information or CSF analysis results were also excluded.

Data collection

A standard format was designed to collect and organize patient test results and electronic medical information. The collected data included crucial patient details, including age, CSF collection date, hospitalization and discharge dates, causative bacteria, and antimicrobial resistance pattern. The information was collected from the hospital registry database and organized using Excel, Microsoft Corporation (version 2023, Redmond, WA, USA). We ensured that the data was kept confidential and accurate throughout the entire process as a top priority.

CSF collection and analysis

The cerebrospinal fluid (CSF) samples, obtained through a lumbar puncture under aseptic conditions, were received and processed within an hour of arrival at the laboratory. In the beginning, Gram-stained smears were prepared. The samples were incubated on blood, chocolate, and MacConkey agar plates at 37 °C with 5% CO2 for 24–48 h. The organisms were identified and validated using automated systems such as VITEK 2 (bioMérieux, Durham, NC, USA) and MicroScan (West Sacramento, CA, USA) [21]. Bacterial meningitis was categorized as community-acquired (CAI) if the patients had not been hospitalized at the onset of the disease and occurred two weeks after discharge from the hospital or four weeks after surgical treatment [22]. It was considered hospital-acquired (HAI) if the diagnosis was made after a minimum of 7 days after hospitalization, with initial hospitalization unrelated to meningitis or sepsis, or the patient underwent surgery within the previous four weeks [23].

Antibiotic susceptibility test

The assessment of antibiotic susceptibility was conducted with the use of the totally automated VITEK system (bioMérieux, Durham, NC, USA). This system conducted minimum inhibitory concentration (MIC) assays and antimicrobial susceptibility testing for various antibiotics comprising beta-lactams (penicillins, carbapenems, cephalosporins, and monobactams), sulfonamides, aminoglycosides, tetracycline, fluoroquinolones, glycopeptides, polymyxins, chloramphenicol, and rifampin. Isolates were classified into four resistance patterns according to standardized definitions. Carbapenem-resistant Enterobacteriaceae (CRE) refers to isolates demonstrating in vitro non-susceptibility to any carbapenem and/or documented carbapenemase production. Extended-spectrum beta-lactamase (ESBL) producers were defined as encoding enzymes capable of hydrolyzing penicillins, first-, second-, and third generation cephalosporins, and monobactams. Methicillin-resistant Staphylococcus aureus (MRSA) denoted isolates with an oxacillin minimum inhibitory concentration (MIC) ≥ 4 µg/mL [24]. Multidrug-resistant (MDR) organisms were categorized as non-susceptible to ≥ 3 antibiotic classes [25]. The Clinical Laboratory Standards Institute (CLSI) guidelines (33rd Edition, 2023) were adhered to during the data analysis and interpretation.

Data quality assurance

One of the authors extracted patient information from medical records into a Microsoft Excel spreadsheet to ensure data quality and integrity. Two additional authors independently validated all extracted data entries by cross-checking with source documents for verification purposes. Any discrepancies between data abstractors were resolved through a joint re-examination of original medical records. Patients with missing medical records were also excluded.

Statistical analysis

The data was structured in a tabular format and analyzed descriptively by calculating means and creating frequency tables. The IBM SPSS version 25 software was utilized to conduct statistical analysis. Univariate analysis was used to investigate individual variables through statistical tests such as chi-squared ($\chi 2$) for categorical variables. Only variables with p-values of 0.05 or less were considered significant predictors.

Ethical approval

The Health Ethics Committee in Jazan, Saudi Arabia, approved the study [number 2328 dated 21/03/2023], and the confidentiality of the collected data was appropriately maintained. The research carried out a secondary analysis of anonymous monitoring data that had been consistently collected. The study followed the ethical policies outlined in the Helsinki Declaration and specific regulations set by the National Committee of Bioethics in Saudi Arabia. Standard clinical methods were employed to obtain data from patient files and laboratory databases without disclosing any personal information of the patients.

Results

During the study, 222 samples were collected from patients with bacterial meningitis at KFCH, all meeting the inclusion criteria. Of these patients, 104 (47%) were children aged 29 days to 17 years, 83 (37%) were adults aged 18 years or older, and 35 (16%) were neonates aged 28 days or younger. Concerning admission location, 112 (50.45%) were reported from all types of ICUs, while 110 (49.55%) were from the wards. Meningitis of hospital origin (HAI) has a more significant proportion than community-acquired infections, with rates of 92% and 8%, respectively. Extended-spectrum beta-lactamase (ESBL) was the most common antibiotic resistance pattern in 12.2% of cases. Carbapenem-resistant Enterobacteriaceae (CRE) and multidrug-resistant organisms (MDRO) were each responsible for 5.4% of cases. MRSA had the lowest frequency rate, representing only 1.4% of cases. Patients were grouped based on length of hospitalization: more than three months (33%), 2–3 months

(30%), and less than two months (32%). The prevalence of bacterial meningitis during the study period from January 2018 to November 2023 was highest in 2020, with 30% of cases, while the lowest rate was observed in 2018, with only 3% of cases. Further details about the patients' characteristics are available in Table 1. *Pseudomonas aeruginosa* accounted for most bacterial meningitis cases (43%), followed by *Klebsiella pneumoniae* (14%). *Proteus mirabilis, Escherichia coli, Serratia marcescens, and Acinetobacter baumannii* accounted for 5% of cases each. The distribution of the causative organisms of bacterial meningitis can be visualized in Fig. 1.

CRE: carbapenem-resistant Enterobacteriaceae. ESBL: extended spectrum beta-lactamase. MDRO: multidrug-resistant organism. MRSA: methicillin-resistant Staphylococcus aureus. CAI: community-acquired infections. HAI: hospital-acquired infections. ND: Not determined. ICU: intensive care unit.

Table 2 indicates that Gram-negative bacteria were the cause of 87% of cases, while Gram-positive bacteria were responsible for 13%. The majority of Gram-negative bacteria were found in ICUs (54%), while wards were the most admission location for Gram-positive bacteria with 71% of cases *(p-value = 0.013)*. Regarding the origin of infections, meningitis of hospital origin (HAI) accounted for the majority of both Gram-negative bacteria and Gram-positive bacteria, with rates of 94% and 75% of cases, respectively *(p-value > 0.005)*. Concerning antimicrobial resistance patterns, ESBLs were reported in 14% of Gram-negative bacteria, followed by MDRO and CRE with 6% of cases for each. Out of 28 cases of Gram-positive bacteria, 11% were reported as MRSA *(p-value > 0.005)*. Length of hospital stay was more than three months for 36% of patients with Gram-negative bacteria and only 11% for those with Gram-positive bacteria *(p-value > 0.005)*.

Table 3 provides additional information about the characteristics of patients and their correlation with antimicrobial resistance patterns. ESBL bacteria were detected in neonates (44%), adults (30%), and children (26%). CRE was found in children (58%) and adults (42%). MDRO

Table 1 Descriptive analysis for the included data based on years 2018–2023

Variable		2018 (*n* = 7, 3%)	2019 (*n* = 22, 10%)	2020 (*n* = 67, 30%)	2021 (*n* = 44, 20%)	2022 (*n* = 47, 21%)	2023 (*n* = 35, 16%)	Total (*n* = 222, 100%)
		n (%)	*n* (%)	*n* (%)	*n* (%)	*n* (%)	*n* (%)	*n* (%)
Age group	Neonates	6 (86)	6 (27%)	11 (16%)	4 (9%)	2 (4%)	6 (17%)	35 (16%)
	Children	1 (14%)	11 (50%)	46 (69%)	18 (41%)	5 (11%)	23 (66%)	104 (47%)
	Adults	0 (0)	5 (23%)	10 (15%)	22 (50)	40 (85%)	6 (17%)	83 (37%)
Location	ICU	6 (86%)	8 (36%)	55 (82%)	18 (41%)	17 (36%)	8 (23%)	112 (50.45%)
	WARD	1 (14%)	14 (64%)	12 (18%)	26 (59%)	30 (64%)	27 (77%)	110 (49.55%)
Origin of infection	CAI	0 (0%)	1 (5%)	4 (6%)	4 (9%)	1 (2%)	8 (23%)	18 (8%)
	HAI	7 (100%)	21 (95%)	63 (94%)	40 (91%)	46 (98%)	27 (77%)	204 (92%)
Alert	*CRE*	0 (0%)	0 (0%)	9 (13%)	0 (0%)	3 (6%)	0 (0%)	12 (5.4%)
	ESBLs	3 (43%)	1 (5%)	8 (12%)	6 (14%)	3 (6%)	6 (17%)	27 (12.2%)
	MDRO	0 (0%)	2 (9%)	0 (0%)	8 (18%)	0 (0%)	2 (6%)	12 (5.4%)
	MRSA	0 (0%)	0 (0%)	1 (1%)	2 (5%)	0 (0%)	0 (0%)	3 (1.4%)
	No alert	4 (57%)	19 (86%)	49 (73%)	28 (64%)	41 (87%)	27 (77%)	168 (75.6%)
Gram stain	Negative	7 (100%)	17 (77%)	61 (91%)	37 (84%)	42 (89%)	30 (86%)	194 (87%)
	Positive	0 (0%)	5 (23%)	6 (9%)	7 (16%)	5 (11%)	5 (14%)	28 (13%)
Length of hospital stay	< 2 months	0 (0%)	5 (23%)	18 (27%)	19 (43%)	17 (36%)	12 (34%)	71 (32%)
	2–3 months	2 (29%)	2 (9%)	49 (73%)	10 (23%)	2 (4%)	1 (3%)	66 (30%)
	> 3 months	5 (71%)	15 (68%)	0 (0%)	15 (34%)	28 (60%)	10 (29%)	73 (33%)
	ND	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	12 (34%)	12 (5%)
Organisms	*Pseudomonas aeruginosa*	1 (14%)	8 (36%)	35 (52%)	18 (41%)	14 (30%)	20 (57%)	96 (43%)
	Klebsiella pneumoniae	3 (43%)	1 (5%)	12 (18%)	10 (23%)	6 (13%)	0 (0%)	32 (14%)
	Proteus mirabilis	0 (0%)	0 (0%)	0 (0%)	0 (0%)	11 (23%)	0 (0%)	11 (5%)
	Escherichia coli	1 (14%)	1 (5%)	3 (4%)	2 (5%)	2 (4%)	1 (3%)	10 (5%)
	Serratia marcescens	0 (0%)	0 (0%)	8 (12%)	0 (0%)	0 (0%)	2 (6%)	10 (5%)
	Acinetobacter baumannii	1 (14%)	2 (9%)	0 (0%)	2 (5%)	3 (6%)	2 (6%)	10 (5%)
	Others	1 (14%)	10 (45%)	9 (13%)	12 (27%)	11 (23%)	10 (29%)	53 (24%)

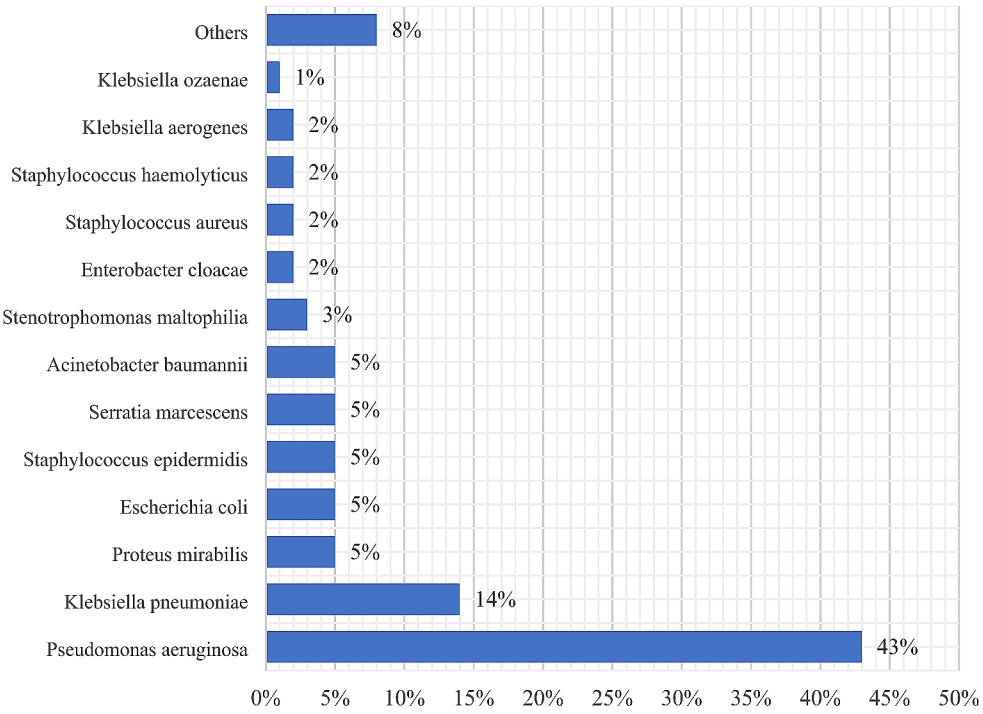

Fig. 1 The most common organisms causing meningitis in this study

Table 2 Variables categorized based on Gram-stain test

Variable		Gram-Negative Bacteria ($n=194$, 87%)	Gram-Positive Bacteria ($n=28$, 13%)	*p*-value
		n (%)	*n* (%)	
Age group	Neonates	33 (17%)	2 (7%)	0.058
	Children	94 (48%)	10 (36%)	
	Adults	67 (35%)	16 (57%)	
Location	ICU	104 (54%)	8 (29%)	0.013
	WARD	90 (46%)	20 (71%)	
Origin	CAI	11 (6%)	7 (25%)	< 0.005
	HAI	183 (94%)	21 (75%)	
Alert	ESBLs	27 (14%)	0 (0%)	< 0.005
	MDRO	12 (6%)	0 (0%)	
	CRE	12 (6%)	0 (0%)	
	MRSA	0 (0%)	3 (11%)	
	No alert	143 (74%)	25 (89%)	
Length of hospital stay	< 2 months	51 (26%)	20 (71%)	< 0.005
	2–3 months	61 (31%)	5 (18%)	
	> 3 months	70 (36%)	3 (11%)	
	ND	12 (6%)	0 (0%)	

CRE: carbapenem-resistant Enterobacteriaceae. ESBL: extended spectrum beta-lactamase. MDRO: multidrug-resistant organism. MRSA: methicillin-resistant Staphylococcus aureus. CAI: community-acquired infections. HAI: hospital-acquired infections. ND: Not determined. ICU: intensive care unit

were isolated in adults (50%) and children (42%). MRSA cases were reported in children (67%) and adults (33%) *(p-value > 0.005)*. CRE were reported in wards (75%), while ESBLs were mostly in ICU (74%). Most MDRO were reported at wards with rates of 58%, followed by ICU with 42% of cases *(p-value = 0.014)*. ESBLs are prevalent in Klebsiella pneumoniae (48%), followed by Escherichia coli (22%) and Klebsiella aerogenes (15%). CRE are reported in Serratia marcescens and Klebsiella pneumoniae with 58% and 42%, respectively. MDRO cases were exhibited in Pseudomonas aeruginosa and Acinetobacter baumannii, with 33% cases each *(p-value > 0.005)*.

Figure 2 illustrates the temporal distribution of bacterial meningitis cases over the period between January 2018 and November 2023. The highest incidence of cases occurred in October (17%) and November (16%). July had the lowest prevalence, recorded at 3%, compared to other months.

Discussion

Over the last three decades, the epidemiology of bacterial meningitis has considerably changed. This change can be attributed to the availability of conjugate vaccines, which target *Haemophilus influenzae type* B, *Streptococcus pneumoniae*, and *Neisseria meningitidis*. Furthermore, pregnant women and individuals with weakened immune systems are now receiving prophylactic antimicrobial therapies as a preventive measure. Due to the considerable morbidity and mortality rates linked to bacterial meningitis, having precise knowledge about the critical causative agents and high-risk populations is crucial for implementing effective public health interventions and ensuring optimal patient care [19, 26]. The primary objective of this study is to examine the trends in the epidemiology of bacterial meningitis among

Table 3 Descriptive analysis for the included data based on their relationship to antimicrobial resistance patterns

Variable		CRE ($n=12$, 5.4%)	ESBLs ($n=27$, 12.2%)	MDRO ($n=12$, 5.4%)	MRSA ($n=3$, 1.4%)	*p*-value
		n (%)	*n* (%)	*n* (%)	*n* (%)	
Age group	Neonates	0 (0%)	12 (44%)	1 (8%)	0 (0%)	< 0.005
	Children	7 (58%)	7 (26%)	5 (42%)	2 (67%)	
	Adults	5 (42%)	8 (30%)	6 (50%)	1 (33%)	
Location	ICU	3 (25%)	20 (74%)	5 (42%)	0 (0%)	0.014
	WARD	9 (75%)	7 (26%)	7 (58%)	3 (100%)	
Origin	CAI	0 (0%)	1 (4%)	0 (0%)	0 (0%)	0.406
	HAI	12 (100%)	26 (96%)	12 (100%)	3 (100%)	
Length of hospital stay	< 2 months	5 (42%)	10 (37%)	7 (58%)	2 (67%)	0.083
	2–3 months	7 (58%)	7 (26%)	3 (25%)	1 (33%)	
	> 3 months	0 (0%)	10 (37%)	2 (17%)	0 (0%)	
	ND	0 (0%)	0 (0%)	0 (0%)	0 (0%)	

CRE: carbapenem-resistant Enterobacteriaceae. ESBL: extended spectrum beta-lactamase. MDRO: multidrug-resistant organism. MRSA: methicillin-resistant Staphylococcus aureus. CAI: community-acquired infections. HAI: hospital-acquired infections. ND: Not determined. ICU: intensive care unit

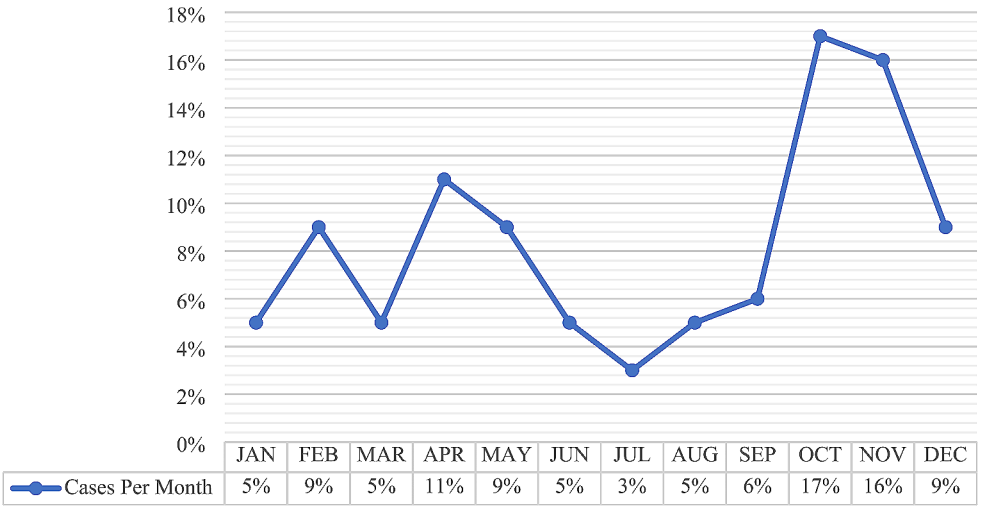

Fig. 2 Distribution of the positive cases of meningitis during the months of the years 2018–2023 ($n=222$)

hospitalized patients in southwestern Saudi Arabia. The investigation is carried out in a facility acknowledged as a referral center and the exclusive venue for neurosurgeries in the region. The discernible variations in the positivity rate across years primarily stem from enhancements in internal protocols governing the handling of CSF samples, guided by insights from treating physicians and laboratory practices. Furthermore, these fluctuations could be linked to local practices, where private or primary centers often resort to antibiotic administration in emergency settings even prior to conducting lumbar punctures. Additionally, the undeniable impact of the COVID-19 pandemic has contributed to these observed variations.

Our study observed a higher incidence of meningitis among pediatric populations, with 63% of cases occurring in neonates and children, consistent with previous observation [27]. The increased vulnerability of children to bacterial meningitis can be attributed to their immature immune systems, specifically their limited ability to combat bacteria commonly associated with this condition [28]. Notably, more than three-quarters of all cases of bacterial meningitis occur in children under the age of five, underscoring the significant impact of this infection in this age group nationally and globally [28, 29]. Moreover, the local practice, characterized by trained pediatricians and the presence of an organized residency and fellowship programs, may exert influence on the quality of the submitted CSF samples and, consequently, impact the obtained positive results. In contrast, adults accounted for a substantial portion of meningitis cases (37%). The elevated susceptibility of adults to bacterial meningitis may originate from various factors, including a higher prevalence of acute and chronic underlying diseases and immunosenescence, which denotes a decline in immune function associated with aging. Notably, epidemiological studies have linked pneumonia, diabetes, renal or hepatic failure, and other chronic conditions with bacterial meningitis in older adults [30–32].

Meningitis caused by Gram-negative rods can be acquired through direct meningeal infection from neurosurgical procedures or trauma. Alternatively, it may result from the hematogenous spread of these organisms come from a distant infection site, such as the urinary tract or abdomen. Adults appear to experience gram-negative meningitis related to these etiologies more frequently than other age groups [33–35]. Our study revealed that HAI constituted the predominant majority (92%) of meningitis cases, in contrast to the 8% observed in the community. This underscores the considerable burden of healthcare-associated meningitis, an anticipated outcome in the singular center responsible for conducting neurosurgeries in the region. The facility handles numerous complex neurosurgical cases, including procedures such as tumor resection and the insertion or alteration of ventriculoperitoneal shunts. Regarding admission location, over half (50.45%) of causative organisms were from ICU patients. Reported nosocomial meningitis incidences vary globally from < 1–7% overall and 0.34-25% post-operatively [10, 36, 37]. Risk factors include invasive neurosurgical procedures, spinal interventions, catheter/device implantation, head trauma, and prolonged ICU stays [14], allowing opportunistic pathogens such as Gram-negative rods to breach central nervous system barriers and establish infection [38]. The predominance of ICU-derived isolates in our cohort likely reflects the vulnerability of critically ill, neurologically complex patients to device-related meningitis. The results of our study contrast with previous reports on the etiology of bacterial meningitis. Our investigation revealed that gram-negative bacteria are the principal causative agents in 87% of bacterial meningitis infections. Specifically, *Pseudomonas aeruginosa* was the leading cause in 43% of cases, which diverges from other reports typically implicating gram-positive *Streptococcus pneumoniae* alongside the gram-negative *Neisseria meningitidis* as predominant etiologies [23, 39]. These differences in findings can be attributed to the nature of the collected data, which predominantly stems from hospitalized patients who are more prone to HAI. Gram-negative rods typically inhabit the gastrointestinal and urogenital tracts and their access to the central nervous system may be facilitated by conditions weakening gut barrier integrity [40]. This disparity may relate to factors increasing Gram-negative bacteremia risk in our locale, including a high prevalence of diabetes, malaria, sickle-cell disease, and other chronic conditions that compromise resistance to infection [41–43]. Also, this increase can be explained by a greater incidence of post-neurosurgical forms, which may be explained by the significant rise in head and spinal cord surgical procedures in recent decades [44]. However, several studies have pointed to increase the frequency of Gram-negative bacterial meningitis over the last decades [45, 46].

In terms of specific etiologies, our identification revealed a bacterial profile typically associated with hospital settings rather than community settings. The most prevalent pathogens were *Pseudomonas aeruginosa, Klebsiella pneumoniae*, and *Escherichia coli*. This pattern differs from trends observed elsewhere, where the impact of *Haemophilus influenzae* type b vaccination often influences prevalence rates [47–53]. Globally, such programs dramatically reduced Hib meningitis [47, 48]. Corresponding shifts towards *Streptococcus pneumoniae* and *Neisseria meningitidis* predominated in children in developed nations and community settings [1, 49–55]. The primary cause of bacterial meningitis was *Pseudomonas aeruginosa*, which accounted for 43% of cases in our findings. *Pseudomonas aeruginosa* is the most frequent cause of nosocomial meningitis [39]. The current study exhibited that 92% of bacterial meningitis cases were HAI, which could explain the high incidence of *Pseudomonas aeruginosa* in this study. However, regional differences may partially explain why our findings depart from this pattern, warranting further exploration of local epidemiological and immunization factors. Compared to previous work, these divergent results highlight the importance of characterizing meningitis etiology within specific geographic contexts.

The results of our study showed significant variability in the incidence of bacterial meningitis during the 6-year study period, with the highest rate observed in 2020 coinciding with the initial COVID-19 pandemic outbreak. This temporal association suggests that containment measures implemented to control SARS-CoV-2 transmission, such as lockdowns and social distancing, have indirectly impacted meningitis epidemiology. This contrasts with reports of declining meningitis cases from hospitals in Germany and China during that time [56, 57]. There are several potential explanations for this observation. First, overall reductions in bacterial respiratory infections following pandemic containment strategies have been documented [58]. Additionally, surveillance data from 26 countries found temporary declines in common respiratory bacteria, including *S. pneumoniae* and *Haemophilus influenzae*, shortly after restrictions began [59]. While the reasons for the increased incidence of meningitis in our study during the pandemic require further exploration, these findings indicate the complex interactions between infectious diseases and public health policies. Additionally, the heightened hospitalization rates and cautious attitudes of healthcare professionals during sample collection may have contributed to a higher positivity rate.

The management of bacterial meningitis of HAI is becoming increasingly challenging due to the growing concern of antimicrobial resistance worldwide. ESBL bacteria were found in 12.2% of the isolates in the present study.

Klebsiella pneumoniae had the highest proportion among ESBL-producing cases, accounting for 48%. These results are low compared to the previous study conducted in China [60]. ESBL *Klebsiella* species have become a significant problem in hospitals due to their high virulence, extraordinary ability to spread, and resistance to multiple antibiotics [61]. CRE was also reported in 5.4% of cases of meningitis in the current study, which played a significant role in neurosurgical bacterial meningitis with strong invasiveness, high toxicity, high morbidity and mortality rates [62]. A small proportion of MRSA cases were identified (1.4%). Patients with prolonged hospitalization and multiple risk factors for MRSA infection, such as central venous or urinary catheters, intubation, or antibiotic therapy, are prone to MRSA meningitis, which is typically a nosocomial infection [63]. However, this low percentage compared to others may be due to the local screening programs for better identification and appropriate intervention needed in such cases.

The study analyzed a six-year dataset from 2018 to 2023, providing evidence of changing trends in meningitis epidemiology in Saudi Arabia. It also showed the common isolation among different age groups and their resistance pattern. Despite that, some limitations still exist in this study. First, this is a retrospective study, and the conclusion mostly depends on the accuracy of the data in the hospital, which may result in selection bias and variation in the healthcare that evolved in the previous years. Second, we did not include all clinical variables related to bacterial meningitis, such as the patient's history and clinical characteristics, molecular characterization of causative agents, and primary clinical laboratory tests were not embedded. Lastly, the study reported a peak in bacterial meningitis cases in 2020, concurrent with the COVID-19 pandemic. The influence of pandemic-related factors on disease incidence and treatment outcomes warrants further investigation to delineate causal relationships.

Future research directions should prioritize a multifaceted approach to address the identified limitations, including the retrospective study design and single-center focus, to enhance the generalizability and depth of understanding. Investigating the underlying mechanisms driving antimicrobial resistance, exploring external factors influencing disease dynamics, and conducting prospective multicenter studies could provide a comprehensive understanding of bacterial meningitis epidemiology in Saudi Arabia. Furthermore, molecular characterization of resistant strains, evaluation of vaccination impact, and continued surveillance to monitor evolving trends are critical for guiding public health strategies and optimizing patient care in managing bacterial meningitis.

Conclusion

In conclusion, our study offers valuable insights into bacterial meningitis's epidemiology and antimicrobial resistance profiles in a Saudi Arabian tertiary hospital setting. Key findings revealed a predominant occurrence of bacterial meningitis in pediatric populations, with a notable vulnerability among neonates and children. The study highlighted a concerning prevalence of nosocomial meningitis, particularly in ICU settings, indicating the significance of healthcare-associated infections in the burden of the disease. The dominance of Gram-negative bacteria as causative agents challenged traditional pathogen trends observed in other regions and emphasized the need for region-specific epidemiological investigations. The temporal variability in meningitis cases, notably the spike in incidence during the initial outbreak of the COVID-19 pandemic, could be related to the potential impact of external factors on disease patterns. The emergence of antimicrobial resistance, notably ESBL, CRE, and MRSA, poses a significant challenge in managing bacterial meningitis, necessitating a focused approach towards surveillance and stewardship to preserve treatment efficacy.

Author contributions Conceptualization and Writing—original draft: A.H.A, K.M.A., B.M.A. A.Y.G., E.F.H., Formal analysis: A.H.A., K.M.A., B.M.A. Writing—review and editing: T.A.Z., A.J.A., E.G.M., W.A.A., R.M.M., A.A.B, A.A.A., N.S.D., M.H. Supervision: A.H.A. All authors have read and agreed to the published version of the manuscript.

Funding This research received no external funding.

Data availability The data presented in this study are available on request from the first author.

Declarations

Institutional review board statement The study was approved by the Jazan Health Ethics Committee (REC) at the Ministry of Health. [number 2328 dated 21/03/2023]

Informed consent Na.

Conflict of interest The authors declare no conflicts of interest.

Competing interests The authors declare no competing interests.

References

1. van de Beek D, de Gans J, Spanjaard L, Weisfelt M, Reitsma JB, Vermeulen M (2004) Clinical features and prognostic factors in adults with bacterial meningitis. N Engl J Med 351(18):1849–1859
2. Robinson CP, Busl KM (2019) Meningitis and encephalitis management in the ICU. Curr Opin Crit Care 25(5):423–429

3. van de Beek D, Cabellos C, Dzupova O, Esposito S, Klein M, Kloek AT et al (2016) ESCMID guideline: diagnosis and treatment of acute bacterial meningitis. Clin Microbiol Infect 22:S37–62
4. Mount HR, Boyle SD (2017) Aseptic and bacterial meningitis: evaluation, treatment, and Prevention. Am Fam Physician 96(5):314–322
5. Blaney SMGAOJ et al (2018) Rudolph's pediatrics. 23rd. McGraw-Hill Education / Medical
6. Ku LC, Boggess KA, Cohen-Wolkowiez M (2015) Bacterial meningitis in infants. Clin Perinatol 42(1):29–45
7. Thigpen MC, Whitney CG, Messonnier NE, Zell ER, Lynfield R, Hadler JL et al (2011) Bacterial meningitis in the United States, 1998–2007. N Engl J Med 364(21):2016–2025
8. Novak RT, Ronveaux O, Bita AF, Aké HF, Lessa FC, Wang X et al (2019) Future directions for Meningitis Surveillance and Vaccine evaluation in the Meningitis Belt of Sub-saharan Africa. J Infect Dis 220(Supplement4):S279–S285
9. Kurtaran B, Kuscu F, Ulu A, Inal AS, Komur S, Kibar F et al (2017) The causes of post-operative meningitis: the comparison of gram-negative and gram-positive pathogens. Turk Neurosurg
10. Hussein K, Bitterman R, Shofty B, Paul M, Neuberger A (2017) Management of post-neurosurgical meningitis: narrative review. Clin Microbiol Infect 23(9):621–628
11. Baer ET, Warltier DC (2006) Post–Dural puncture bacterial meningitis. Anesthesiology 105(2):381–393
12. Baltas I, Tsoulfa S, Sakellariou P, Vogas V, Fylaktakis M, Kondodimou A (1994) Posttraumatic Meningitis Neurosurg 35(3):422–427
13. Hoogmoed J, van de Beek D, Coert BA, Horn J, Vandertop WP, Verbaan D (2017) Clinical and Laboratory characteristics for the diagnosis of bacterial ventriculitis after Aneurysmal Subarachnoid Hemorrhage. Neurocrit Care 26(3):362–370
14. van de Beek D, Drake JM, Tunkel AR (2010) Nosocomial bacterial meningitis. N Engl J Med 362(2):146–154
15. Shukla B, Aguilera EA, Salazar L, Wootton SH, Kaewpoowat Q, Hasbun R (2017) Aseptic meningitis in adults and children: diagnostic and management challenges. J Clin Virol 94:110–114
16. Park SE, Lim TJ, Nam SO, Chang CL, Byun SY, Ko A et al (2020) Clinical utility of the FilmArray meningitis/encephalitis panel in children at a tertiary center in South Korea. Brain Dev 43(2):234–243
17. Liu BM, Mulkey SB, Campos JM, DeBiasi RL (2024) Laboratory diagnosis of CNS infections in children due to emerging and re-emerging neurotropic viruses. Pediatr Res 95(2):543–550
18. Sunnerhagen T, Widén J, Handhal S, Özkaya Şahin G (2024) A retrospective observational study of 1000 consecutive patients tested with the FilmArray® Meningitis/Encephalitis panel: clinical diagnosis at discharge and microbiological findings. Sci Rep 14(1):4015
19. Brouwer MC, van de Tunkel AR (2010) Epidemiology, diagnosis, and Antimicrobial Treatment of Acute bacterial meningitis. Clin Microbiol Rev 23(3):467–492
20. Kabra SK, Kumar P, Verma IC, Mukherjee D, Chowdhary BH, Sengupta S et al (1991) Bacterial meningitis in India: an IJP survey. Indian J Pediatr 58(4):505–511
21. Alhazmi AH, Alameer KM, Abuageelah BM, Alharbi RH, Mobarki M, Musawi S et al (2023) Epidemiology and antimicrobial resistance patterns of urinary tract infections: a cross-sectional study from Southwestern Saudi Arabia. Med (B Aires) 59(8):1411
22. Matulyte E, Kiveryte S, Paulauskiene R, Liukpetryte E, Vaikutyte R, Matulionyte R (2020) Retrospective analysis of the etiology, clinical characteristics and outcomes of community-acquired bacterial meningitis in the University Infectious diseases Centre in Lithuania. BMC Infect Dis 20(1):733
23. Elsaid MF, Flamerzi AA, Bessisso MS, Elshafie SS (2006) Acute bacterial meningitis in Qatar. Saudi Med J 27(2):198–204
24. Cag Y, Caskurlu H, Fan Y, Cao B, Vahaboglu H (2016) Resistance mechanisms. Ann Transl Med 4(17):326
25. Magiorakos AP, Srinivasan A, Carey RB, Carmeli Y, Falagas ME, Giske CG et al. (2012) Multidrug-resistant, extensively drug-resistant and pandrug-resistant bacteria: an international expert proposal for interim standard definitions for acquired resistance. Clin Microbiol Infect 18(3):268–281
26. Brouwer MC, van de Beek D (2018) Epidemiology of community-acquired bacterial meningitis. Curr Opin Infect Dis 31(1):78–84
27. Castelblanco RL, Lee M, Hasbun R (2014) Epidemiology of bacterial meningitis in the USA from 1997 to 2010: a population-based observational study. Lancet Infect Dis 14(9):813–819
28. Makwana N, Riordan FAI (2007) Bacterial meningitis. CNS Drugs 21(5):355–366
29. Agrawal S, Nadel S (2011) Acute bacterial meningitis in infants and children. Pediatr Drugs 13(6):385–400
30. Nieman RE, Lorber B (1980) Listeriosis in adults: a changing pattern. Report of eight cases and review of the literature, 1968–1978. Clin Infect Dis 2(2):207–227
31. Cabellos C, Viladrich PF, Corredoira J, Verdaguer R, Ariza J, Gudiol F (1999) Streptococcal meningitis in adult patients: current epidemiology and clinical spectrum. Clin Infect Dis 28(5):1104–1108
32. Domingo P, Barquet N, Alvarez M, Coll P, Nava J, Garau J (1997) Group B streptococcal meningitis in adults: report of twelve cases and review. Clin Infect Dis 25(5):1180–1187
33. Choi C (1992) Bacterial meningitis. Clin Geriatr Med 8(4):889–902
34. Roos KL TASWMSWWRDDT (1997) Acute bacterial meningitis in children and adults, infections of the central nervous system. Lippincott Williams & Wilkins, pp 335–402
35. Berk Sl MWR (1980) Meningitis caused by Gram-Negative Bacilli. Ann Intern Med 93(2):253–260
36. Governale LS, Fein N, Logsdon J, Black PM, Techniques and complications of external lumbar drainage for normal pressure hydrocephalus (2008) Operative Neurosurg 63(4):379–384
37. Palabiyikoglu I, Tekeli E, Cokca F, Akan O, Unal N, Erberktas I et al (2006) Nosocomial meningitis in a university hospital between 1993 and 2002. J Hosp Infect 62(1):94–97
38. Erdem I, Hakan T, Ceran N, Metin F, Akcay S, Kucukercan M et al (2008) Clinical features, laboratory data, management and the risk factors that affect the mortality in patients with postoperative meningitis. Neurol India 56(4):433
39. Pomar V, Benito N, López-Contreras J, Coll P, Gurguí M, Domingo P (2013) Spontaneous gram-negative bacillary meningitis in adult patients: characteristics and outcome. BMC Infect Dis 13(1):451
40. Peltola H, Roine I, Kallio M, Pelkonen T (2022) Unusual gram-negative bacteria cause more severe bacterial meningitis than the three classical agents in children. Acta Paediatr 111(7):1404–1411
41. Hamali HA, Mobarki AA, Saboor M, Alfeel A, Madkhali AM, Akhter MS et al (2020) Prevalence of Anemia among Jazan University students. Int J Gen Med 13:765–770
42. Hazzazi A, Ageeli M, Alfaqih A, Jaafari A, Malhan H, Bakkar M (2020) Epidemiology and characteristics of sickle cell patients admitted to hospitals in Jazan region, Saudi Arabia. J Appl Hematol 11(1):10
43. Al-Mekhlafi HM, Madkhali AM, Ghailan KY, Abdulhaq AA, Ghzwani AH, Zain KA et al (2021) Residual malaria in Jazan region, southwestern Saudi Arabia: the situation, challenges and climatic drivers of autochthonous malaria. Malar J 20(1):315
44. Lu CH, Chang WN, Chuang YC (1999) Resistance to third-generation cephalosporins in adult gram-negative bacillary meningitis. Infection 27(3):208–211

45. Lu CH, Chang WN, Chuang YC, Chang HW (1998) The prognostic factors of adult Gram-negative bacillary meningitis. J Hosp Infect 40(1):27–34
46. O'Neill E, Humphreys H, Phillips J, Smyth EG (2006) Third-generation cephalosporin resistance among Gram-negative bacilli causing meningitis in neurosurgical patients: significant challenges in ensuring effective antibiotic therapy. J Antimicrob Chemother 57(2):356–359
47. Dery M, Hasbun R (2007) Changing epidemiology of bacterial meningitis. Curr Infect Dis Rep 9(4):301–307
48. Schuchat A, Robinson K, Wenger JD, Harrison LH, Farley M, Reingold AL et al (1997) Bacterial meningitis in the United States in 1995. N Engl J Med 337(14):970–976
49. Berg S, Trollfors B, Claesson BA, Alestig K, Gothefors L, Hugosson S et al (1996) Incidence and prognosis of Meningitis due to Haemophilus influenzae, Streptococcus pneumoniae and Neisseria meningitidis in Sweden. Scand J Infect Dis 28(3):247–252
50. Giorgi Rossi P, Mantovani J, Ferroni E, Forcina A, Stanghellini E, Curtale F et al (2009) Incidence of bacterial meningitis (2001–2005) in Lazio, Italy: the results of a integrated surveillance system. BMC Infect Dis 9(1):13
51. Mishal J, Embon A, Darawshe A, Kidon M, Magen E (2008) Community acquired acute bacterial meningitis in children and adults: an 11-year survey in a community hospital in Israel. Eur J Intern Med 19(6):421–426
52. Sigurdardóttir B (1997) Acute bacterial meningitis in adults. Arch Intern Med 157(4):425
53. Theodoridou MN, Vasilopoulou VA, Atsali EE, Pangalis AM, Mostrou GJ, Syriopoulou VP et al (2007) Meningitis registry of hospitalized cases in children: epidemiological patterns of acute bacterial meningitis throughout a 32-year period. BMC Infect Dis 7(1):101
54. Urwin G, Yuan MF, Feldman RA (1994) Prospective study of bacterial meningitis in North East Thames region, 1991-3, during introduction of Haemophilus influenzae vaccine. BMJ 309(6966):1412–1414
55. Weiss DP, Coplan P, Guess H (2001) Epidemiology of bacterial meningitis among children in Brazil, 1997–1998. Rev Saude Publica 35(3):249–255
56. Völk S, Pfirrmann M, Koedel U, Pfister HW, Lang T, Scheibe F et al (2022) Decline in the number of patients with meningitis in German hospitals during the COVID-19 pandemic. J Neurol 269(7):3389–3399
57. Cheng P, Li L, Sun H, Zhu C (2023) Changes of pathogen distribution in children with bacterial meningitis before and after the COVID-19 pandemic in Zhengzhou, China. J Infect 86(3):256–308
58. Amin-Chowdhury Z, Aiano F, Mensah A, Sheppard CL, Litt D, Fry NK et al (2021) Impact of the Coronavirus Disease 2019 (COVID-19) pandemic on invasive pneumococcal disease and risk of pneumococcal coinfection with severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2): prospective National Cohort Study, England. Clin Infect Dis 72(5):e65–75
59. Brueggemann AB, van Jansen MJ, Shaw D, McCarthy ND, Jolley KA, Maiden MCJ et al (2021) Changes in the incidence of invasive disease due to Streptococcus pneumoniae, Haemophilus influenzae, and Neisseria meningitidis during the COVID-19 pandemic in 26 countries and territories in the invasive respiratory infection Surveillance Initiative: a prospective analysis of surveillance data. Lancet Digit Health 3(6):e360–e370
60. Zheng G, Cao Y, Liu C, Qian L, Cai Y, Cui M et al (2021) Phenotype, molecular characterisation and risk factors for postoperative meningitis caused by ESBL-producing-Enterobacteriaceae: a six years multi-centre comparative cohort study. BMC Infect Dis 21(1):85
61. Mengistu A, Gaeseb J, Uaaka G, Ndjavera C, Kambyambya K, Indongo L et al (2013) Antimicrobial sensitivity patterns of cerebrospinal fluid (CSF) isolates in Namibia: implications for empirical antibiotic treatment of meningitis. J Pharm Policy Pract 6(1):4
62. Guanghui Z, Jing L, Guojun Z, Hong L (2020) Epidemiology and risk factors of neurosurgical bacterial meningitis/encephalitis induced by carbapenem resistant Enterobacteriaceae. J Infect Chemother 26(1):101–106
63. Pintado V, Pazos R, Jiménez-Mejías ME, Rodríguez-Guardado A, Gil A, García-Lechuz JM et al (2012) Methicillin-resistant Staphylococcus aureus meningitis in adults. Medicine 91(1):10–17